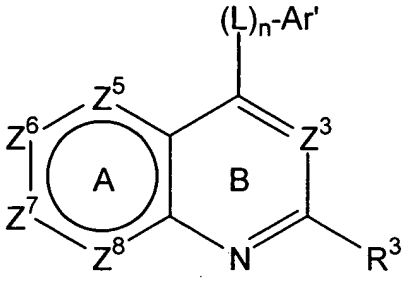
In the Claims

1. (Currently Amended): A method to inhibit p38α activity, which method comprises contacting said p38α with a compound of the formula:



(1)

or the pharmaceutically acceptable salts thereof

wherein R^3 comprises a substituted or unsubstituted aromatic moiety, wherein said aromatic moiety is a monocyclic or fused bicyclic moiety containing 5-12 ring member atoms, optionally comprising one or more heteroatoms selected from O, S and N;

wherein Z^3 is N, Z^5 is CH, and Z^6 and Z^7 are CR^2 ~~and each remaining Z is CR^2 or N, wherein no more than two Z positions in ring A are N, and wherein two adjacent Z positions in ring A cannot be N;~~

Z^8 is CH or N;

each R^2 is either

(i) independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, acyl, wherein each of alkyl, alkenyl, alkynyl and acyl may optionally contain 1-2 O, S or N, aryl, and arylalkyl, each of said aryl and arylalkyl optionally containing 1 or more O, S or N and wherein in each of the foregoing other than H may be unsubstituted or substituted with 1-3 substituents selected independently from the group consisting of alkyl, alkenyl, alkynyl, aryl, alkylaryl, aroyl, N-aryl, NH-alkylaryl, NH-aroyl, halo, OR, NR_2, SR, -SOR, $-SO_2R$, -OCOR, -NRCOR, $-NRCONR_2$, -NRCOOR, -NRSOR, $-NRSO_2R$, $-OCONR_2$, RCO, -COOR, $-SO_3R$, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or alkyl (1-4C), and wherein any aryl or aroyl groups on said substituents may be further substituted by alkyl, alkenyl, alkynyl, halo, OR, NR_2, SR, -SOR, $-SO_2R$, -OCOR, -NRCOR, $-NRCONR_2$, -NRCOOR, -NRSOR, $-NRSO_2R$, $-OCONR_2$, RCO, -COOR, $-SO_3R$, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or alkyl (1-4C), or

(ii) independently selected from the group consisting of halo, OR, NR_2, SR, -SOR, $-SO_2R$, -OCOR, -NRCOR, $-NRCONR_2$, -NRCOOR, NRSOR, $NRSO_2R$, $-OCONR_2$, RCO, -COOR, $-SO_3R$, NRSOR, $NRSO_2R$, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or alkyl (1-4C);

wherein L is $R^1N(CH_2)_n$ wherein R^1 is H, alkyl (1-6C) or arylalkyl optionally substituted on the aryl moiety with 1-3 substituents independently selected from the group consisting of alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or alkyl (1-4C); ~~a divalent moiety that provides a distance of 2-8Å between ring B and Ar';~~

n is 0 or 1; and

(a) Ar' is phenyl, substituted with at least one group selected from the group consisting of optionally substituted alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C), or pyridyl, indolyl, or pyrimidyl, each optionally substituted with at least one group selected from the group consisting of optionally substituted alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C); and

R^3 is phenyl optionally substituted with 1-3 substituents which substituents are selected from the group consisting of alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, $-SO_2NR_2$, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C); or

(b) Ar' is phenyl, pyridyl, indolyl, or pyrimidyl, each optionally substituted with a group selected from the group consisting of optionally substituted alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C); and

R^3 is phenyl substituted with 1-3 substituents which substituents are selected from the group consisting of alkyl (1-6C), halo, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, $-SO_2NR_2$, CN, and CF_3, wherein each R is independently H or lower alkyl (1-4C); or

(c) Ar' is phenyl substituted with a group selected from the group consisting of optionally substituted NR_2, SR, -NROCR, RCO, $-CONR_2$, SO_2NR_2, CN, and CF_3, wherein each R is independently H or lower alkyl (1-4C); or pyridyl substituted with a group selected from the group

consisting of optionally substituted alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C); or indolyl or pyrimidyl, each optionally substituted with a group selected from the group consisting of optionally substituted alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C); and

R^3 is phenyl optionally substituted with 1-3 substituents which substituents are selected from the group consisting of alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, $-SO_2NR_2$, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C); or

(d) Ar′ is phenyl, pyridyl, indolyl, or pyrimidyl, each optionally substituted with a group selected from the group consisting of optionally substituted alkyl (1-6C), halo, OR, NR_2, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C); and

R^3 is phenyl substituted with 1-3 substituents which substituents are selected from the group consisting of alkyl (1-6C), halo, OR, SR, -OOCR, -NROCR, RCO, -COOR, $-CONR_2$, $-SO_2NR_2$, CN, CF_3, and NO_2, wherein each R is independently H or lower alkyl (1-4C).

~~Ar′ is a cyclic hydrocarbyl aliphatic, cyclic hydrocarbyl aliphatic containing one or more heteroatoms or a monocyclic or polycyclic aromatic moiety any of the foregoing optionally substituted with 1-3 substituents, wherein two of said substituents may form a 5-7 member cyclic optionally heterocyclic aliphatic ring and wherein Ar′ and any said substituents thereon forming a cyclic aliphatic ring, may optionally contain one or more ring atoms selected from O, S and N, wherein said compound inhibits p38α activity.~~

2-7. (canceled)

8. (previously presented): The method of claim 1 wherein any substituents on the aromatic or heteroaromatic moiety of R^3 are independently selected from the group consisting of halo, OR, NR_2, SR, -SOR, $-SO_2R$, -OCOR, -NRCOR, $-NRCONR_2$, -NRCOOR, -NRSOR,

-$NRSO_2R$, -$OCONR_2$, RCO, -COOR, -SO_3R, -$CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or alkyl (1-4C) and alkyl (1-6C).

9. (original): The method of claim 1 wherein said substituents on substituted Ar' are independently selected from the group consisting of optionally substituted alkyl, alkenyl, alkynyl, aryl, alkylaryl, aroyl, N-aryl, NH-alkylaryl, NH-aroyl, halo, OR, NR_2, SR, -SOR, -SO_2R, -OCOR, -NRCOR, -$NRCONR_2$, -NRCOOR, -NRSOR, -$NRSO_2R$, -$OCONR_2$, RCO, -COOR, -SO_3R, -$CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or alkyl (1-4C),

and wherein any aryl or aroyl groups on said substituents may be further substituted by alkyl, alkenyl, alkynyl, halo, OR, NR_2, SR, -SOR, -SO_2R, -OCOR, -NRCOR, -$NRCONR_2$, -NRCOOR, -NRSOR, -$NRSO_2R$, -$OCONR_2$, RCO, -COOR, -SO_3R, -$CONR_2$, SO_2NR_2, CN, CF_3, and NO_2, wherein each R is independently H or alkyl (1-4C).

10. (previously presented): The method of claim 9 wherein Ar' is phenyl, 2-, 3-, or 4-pyridyl, 2- or 4-pyrimidyl, indolyl, isoquinolyl, quinolyl, benzimidazolyl, benzotriazolyl, benzothiazolyl, benzofuranyl, pyridyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl, all of which may optionally be substituted.

11-12. (canceled)

13. (previously amended): The method of claim 1 wherein said optional substituents on R^2 are independently selected from the group consisting of R^4, halo, OR^4, NR^4_2, SR^4, -$OOCR^4$, -$NROCR^4$, -$COOR^4$, R^4CO, -$CONR^4_2$, -$SO_2NR^4_2$, CN, CF_3, and NO_2, wherein each R^4 is independently H, or optionally substituted alkyl (1-6C), or optionally substituted arylalkyl (7-12C) and wherein two R^4 or two substituents on said alkyl or arylalkyl taken together may form a fused aliphatic ring of 5-7 members.

14-15. (canceled)

16. (currently amended): The method of claim 1 wherein the compound of formula (1) is selected from group consisting of

(a) the compounds listed in Table 2 below, ~~wherein Z^5-Z^8 are CH~~; Z^3 is N; R^1 in compound No. 11 is 2-propyl; R^1 in compound No. 12 is 4-methoxyphenyl, and R^1 in compound No. 41 is 4-methoxybenzyl; and wherein L, Ar' and R^3 are as shown in Table 2:

Table 2

Compound No.	L	Ar'	R^3
1	NH	4-pyridyl	2-chlorophenyl
2	NH	4-pyridyl	2,6-dichlorophenyl
3	NH	4-pyridyl	2-methylphenyl
4	NH	4-pyridyl	2-bromophenyl
5	NH	4-pyridyl	2-fluorophenyl
6	NH	4-pyridyl	2,6-difluorophenyl
7	NH	4-pyridyl	phenyl
8	NH	4-pyridyl	4-fluorophenyl
9	NH	4-pyridyl	4-methoxyphenyl
10	NH	4-pyridyl	3-fluorophenyl
11	NR^1	4-pyridyl	phenyl
12	NR^1	4-pyridyl	phenyl
13	$NHCH_2$	4-pyridyl	phenyl
14	$NHCH_2$	4-pyridyl	4-chlorophenyl
15	NH	3-pyridyl	phenyl
16	$NHCH_2$	2-pyridyl	phenyl
17	$NHCH_2$	3-pyridyl	phenyl
18	$NHCH_2$	2-pyridyl	phenyl
19	$NHCH_2CH_2$	2-pyridyl	phenyl
20	NH	6-pyrimidinyl	phenyl
21	NH	2-pyrimidinyl	phenyl
22	NH	Phenyl	phenyl
23	$NHCH_2$	Phenyl	3-chlorophenyl
24	NH	3-hydroxyphenyl	phenyl
25	NH	2-hydroxyphenyl	phenyl
26	NH	4-hydroxyphenyl	phenyl

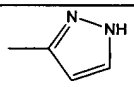
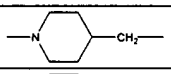
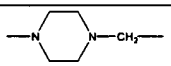
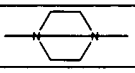
Table 2			
Compound No.	L	Ar'	R^3
27	NH	4-indolyl	phenyl
28	NH	5-indolyl	phenyl
29	NH	4-methoxyphenyl	phenyl
30	NH	3-methoxyphenyl	phenyl
31	NH	2-methoxyphenyl	phenyl
32	NH	4-(2-hydroxyethyl)phenyl	phenyl
33	NH	3-cyanophenyl	phenyl
34	$NHCH_2$	2,5-difluorophenyl	phenyl
35	NH	4-(2-butyl)phenyl	phenyl
36	$NHCH_2$	4-dimethylaminophenyl	phenyl
38	NH	2-pyridyl	phenyl
39	$NHCH_2$	3-pyridyl	phenyl
40	NH	4-pyrimidyl	phenyl
41	NR^1	4-pyridyl	phenyl
42	NH	p-aminomethylphenyl	phenyl
43	$NHCH_2$	4-aminophenyl	phenyl
44	NH	4-pyridyl	3-chlorophenyl
45	NH	Phenyl	4-pyridyl
46	NH		phenyl
48	NH	2-benzylamino-3-pyridyl	phenyl
49	NH	2-benzylamino-4-pyridyl	phenyl
50	NH	3-benzyloxyphenyl	phenyl
51	NH	4-pyridyl	3-aminophenyl
52	NH	4-pyridyl	4-pyridyl
53	NH	4-pyridyl	2-naphthyl
54		4-pyridyl	phenyl
55		Phenyl	phenyl
~~56~~		~~2-pyridyl~~	~~phenyl~~
61	NH	4-pyridyl	2-trifluoromethyl phenyl
62	NH	4-aminophenyl	phenyl

Table 2			
Compound No.	**L**	**Ar'**	**R^3**
64	NH	3-methoxyphenyl	2-fluorophenyl
65	NH	4-methoxyphenyl	2-fluorophenyl
66	NH	4-pyrimidinyl	2-fluorophenyl
67	NH	3-amino-4-pyridyl	phenyl
68	NH	4-pyridyl	2-benzylaminophenyl
69	NH	2-benzylaminophenyl	phenyl
70	NH	2-benzylaminophenyl	4-cyanophenyl
71	NH	3'-cyano-2-benzylaminophenyl	phenyl

(b) the compounds listed in Table 3, below, wherein L is NH; Z^3 is N; Z^6 and Z^7 are CH and Z^5, Z^8, Ar' and R^3 are as shown in Table 3:

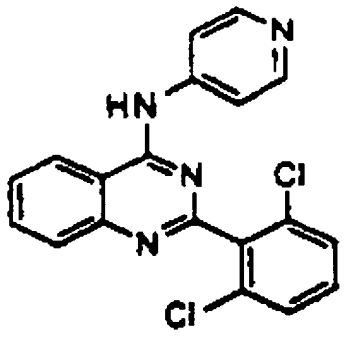
Table 3				
Compound No.	**Z^5**	**Z^8**	**Ar'**	**R^3**
72	CH	N	4-pyridyl	2-fluorophenyl
73	CH	N	4-pyridyl	2-chlorophenyl
74	CH	N	4-pyridyl	phenyl
~~75~~	~~N~~	~~N~~	~~4-pyridyl~~	~~phenyl~~
~~76~~	~~N~~	~~CH~~	~~4-pyridyl~~	~~phenyl~~

and

(c) the quinazoline derivatives listed in Table 4 below, wherein L is NH; Ar' is 4-pyridyl; Z^3, **[[Z^5,]]** and Z^8 are N; Z^5 is CH, Z^6 or Z^7 are CR^2 as shown and each is otherwise N and wherein R^3 and R^2 are as shown in Table 4:

Table 4		
Compound No.	R^3	R^2
77	2-chlorophenyl	6,7-dimethoxy
78	2-fluorophenyl	6-nitro
79	2-fluorophenyl	6-amino
80	2-fluorophenyl	7-amino
81	2-fluorophenyl	6-(3-methoxybenzylamino)
82	2-fluorophenyl	6-(4-methoxybenzylamino)
83	2-fluorophenyl	6-(2-isobutylamino)
84	2-fluorophenyl	6-(4-methylmercaptobenzylamino)
85	2-fluorophenyl	6-(4-methoxybenzoyl amino)
86	4-fluorophenyl	7-amino
87	4-fluorophenyl	7-(3-methoxybenzylamino)

17. (previously presented): The method of claim 1 wherein the compound of formula (1) is selected from the group consisting of the following compounds: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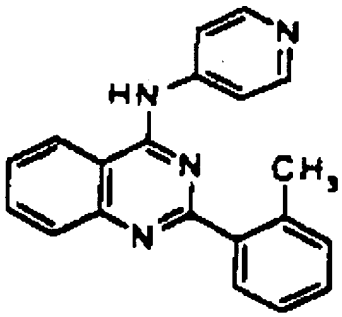
Cl
N
Cl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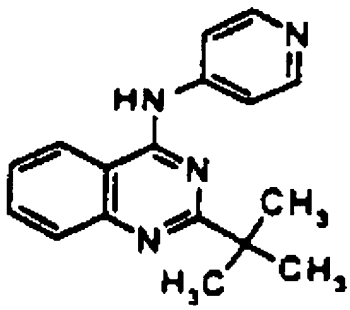
N
CH3
N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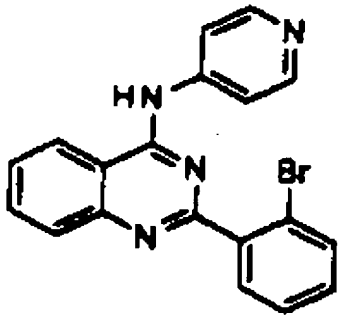
CH3
N
H3C
CH3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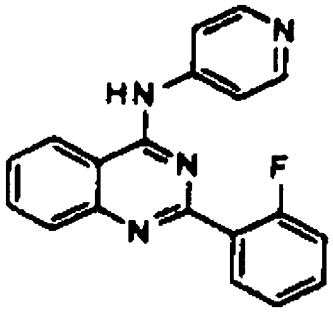
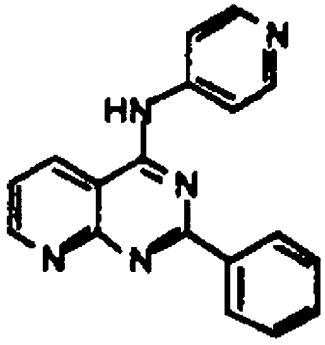
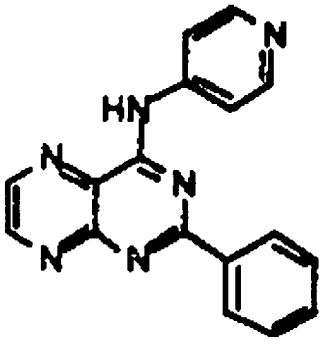
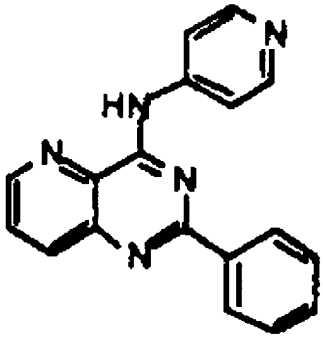
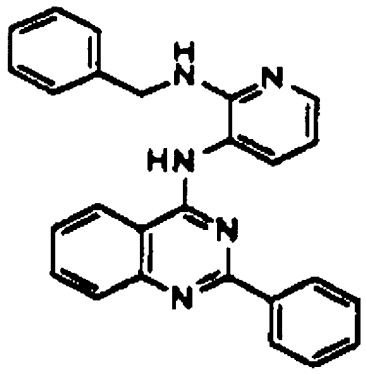
HN
N
Br
N

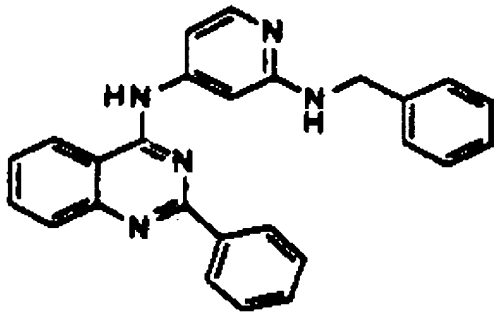


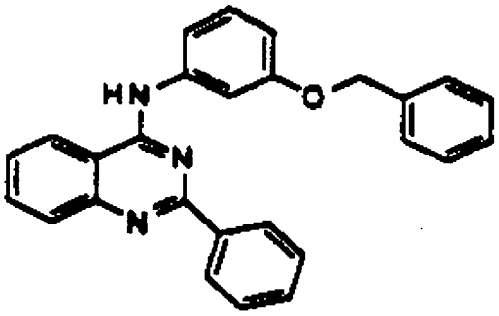


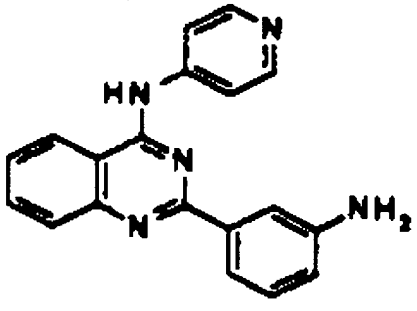


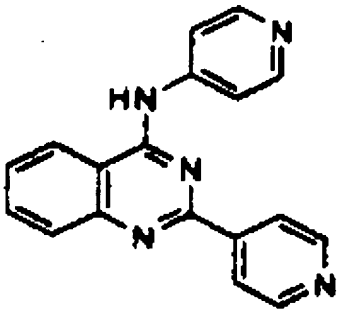


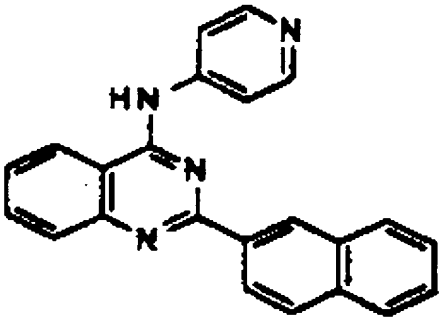


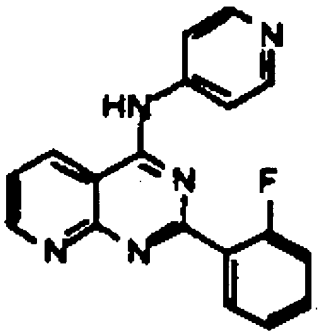


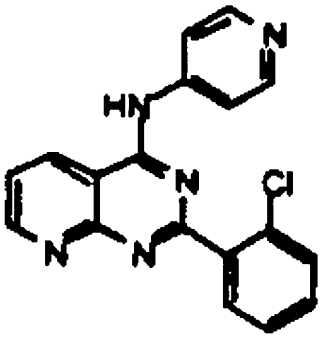


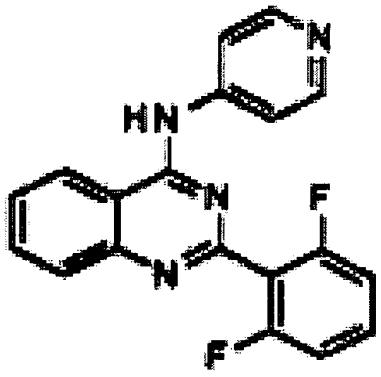








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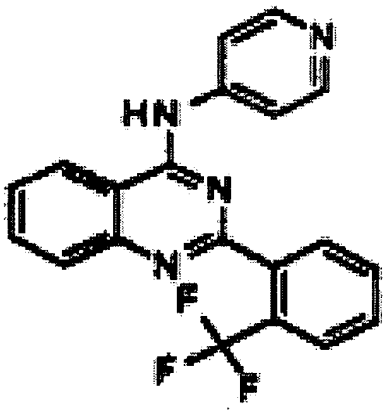
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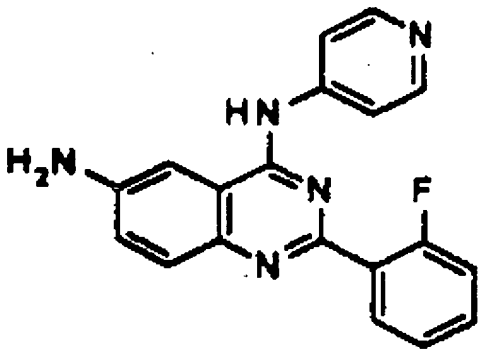

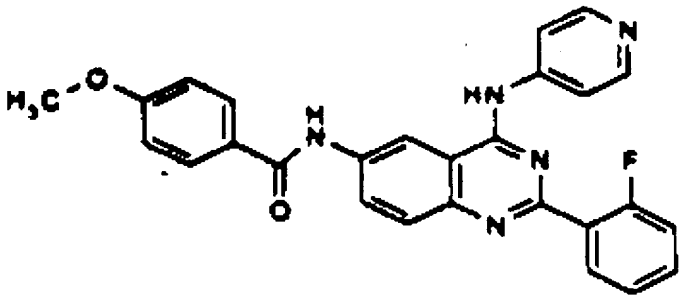

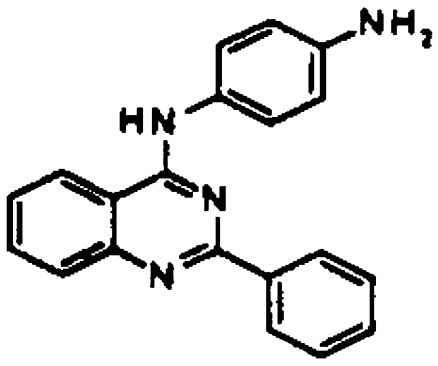

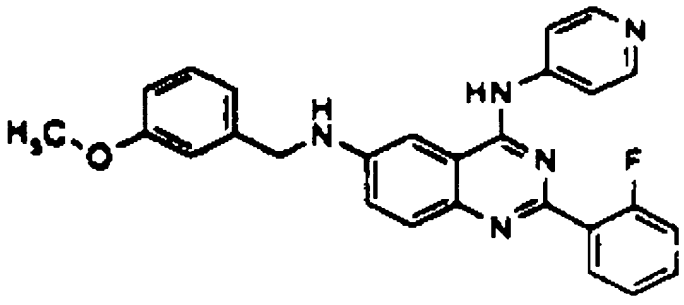

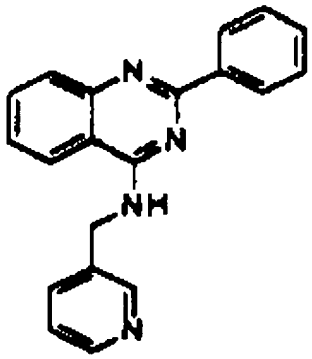

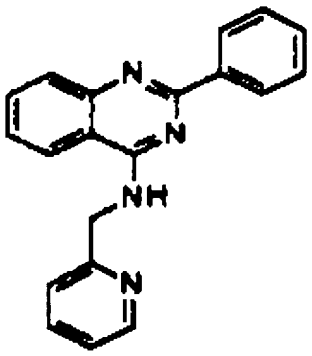

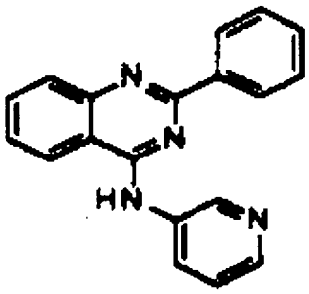

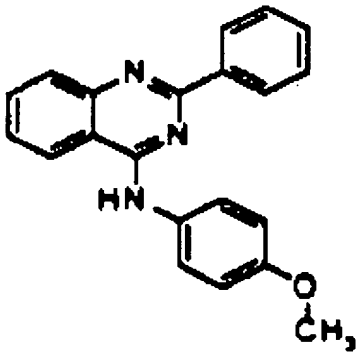

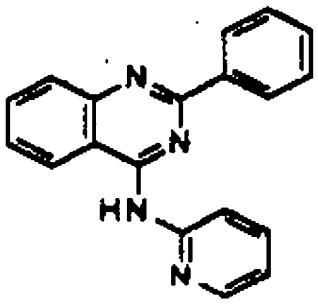

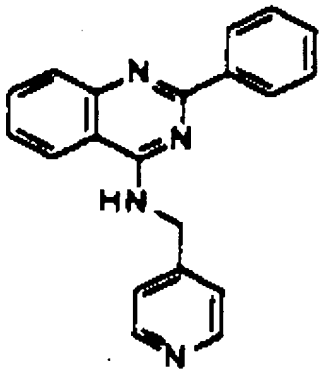

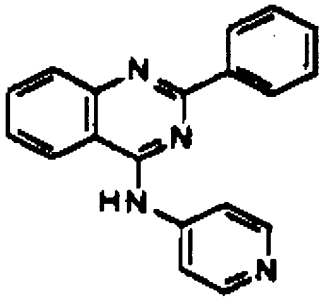

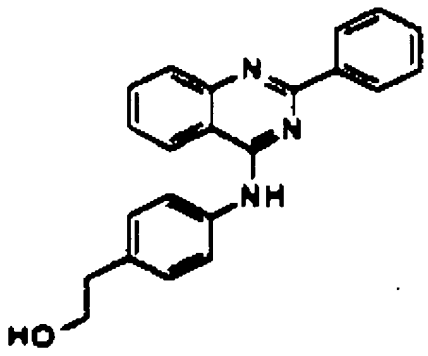

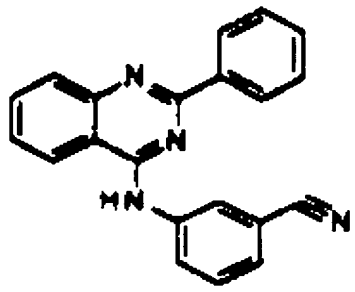

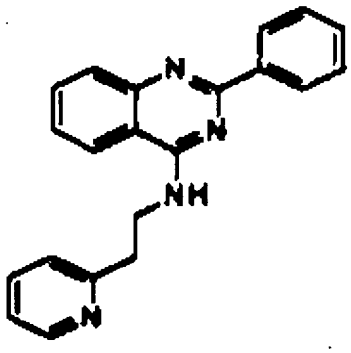

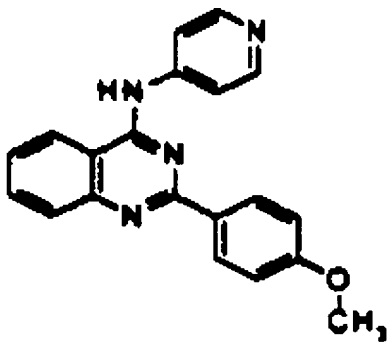

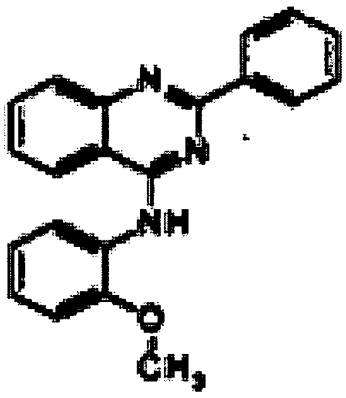

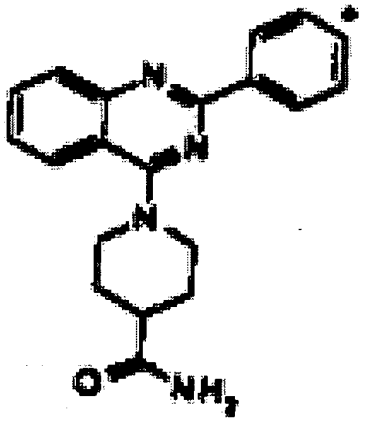

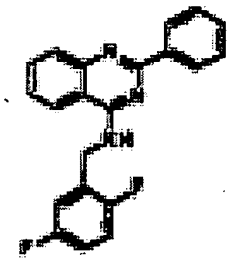

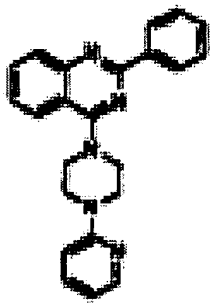

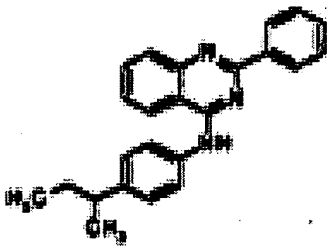

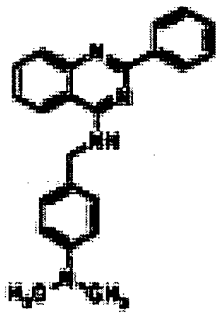

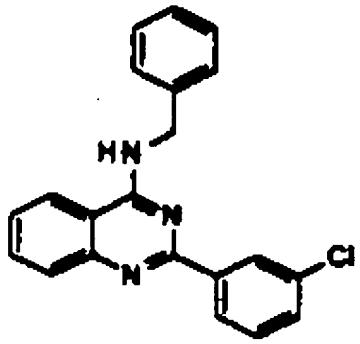

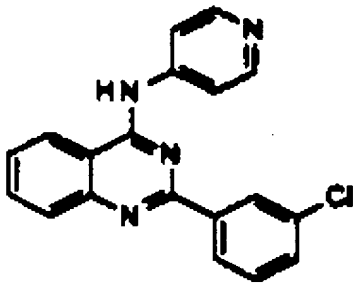

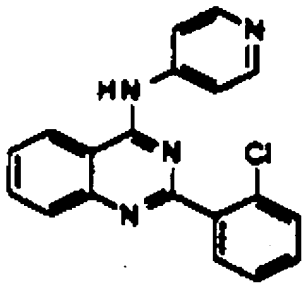

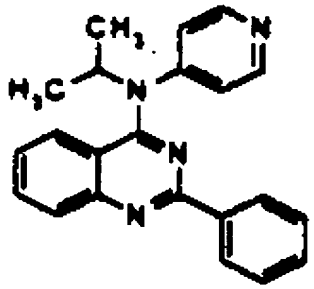

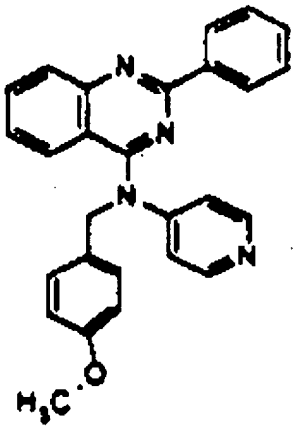

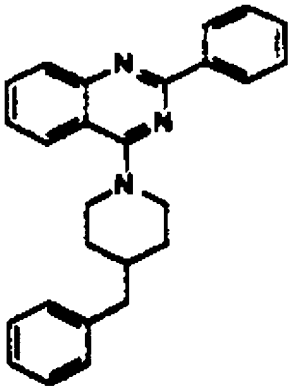

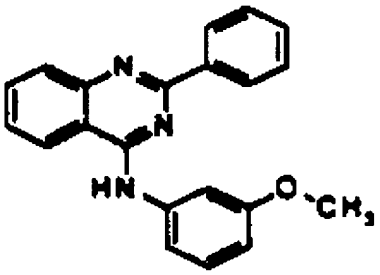

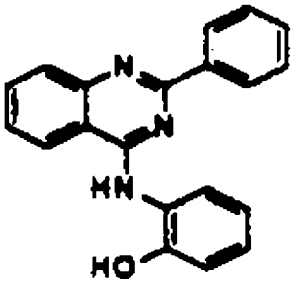

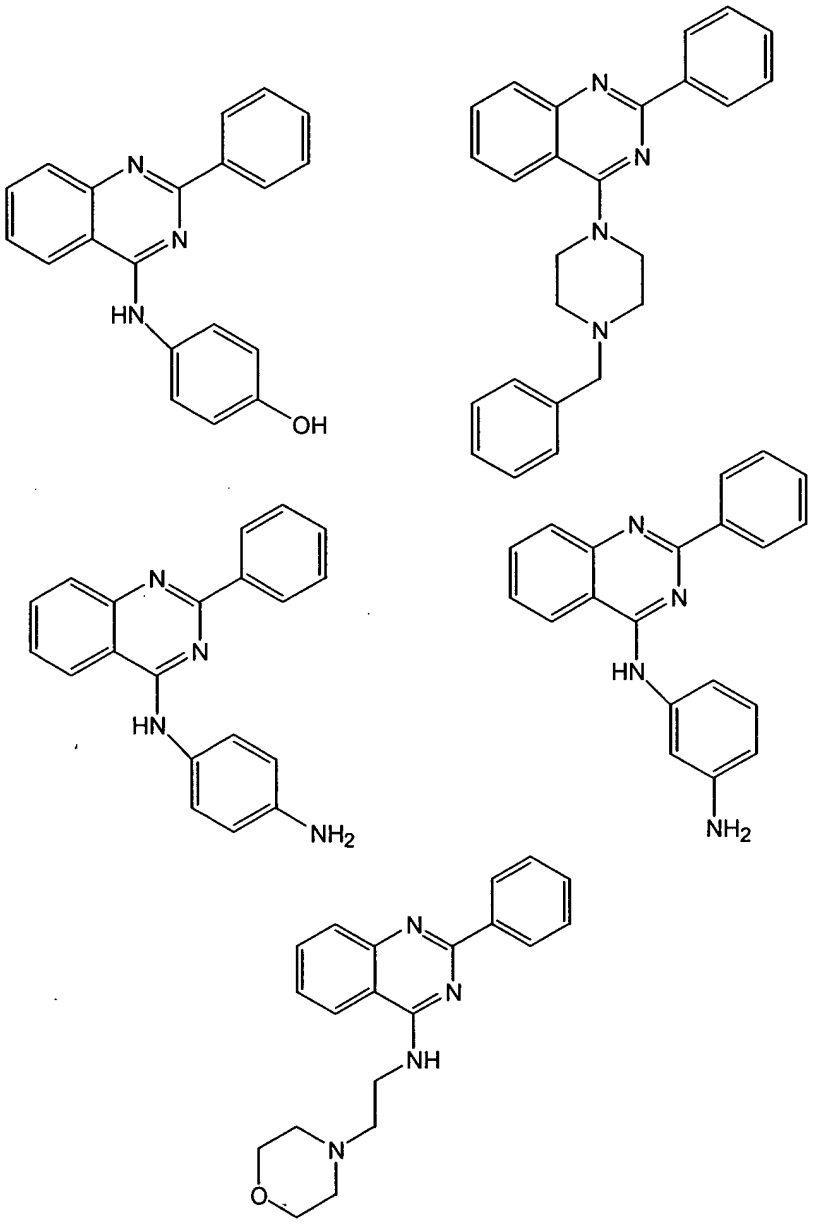

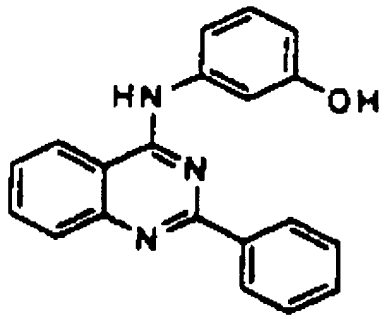
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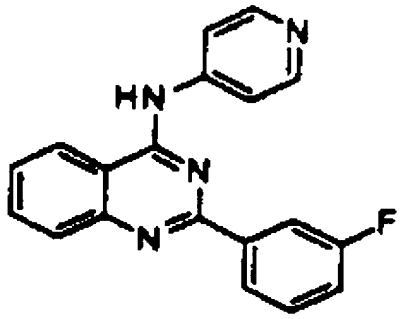
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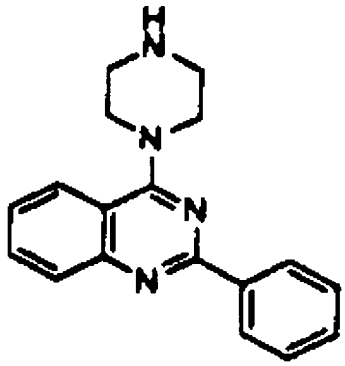
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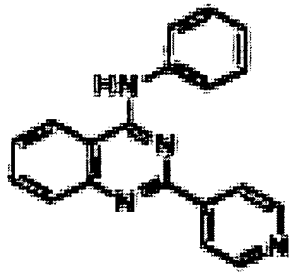

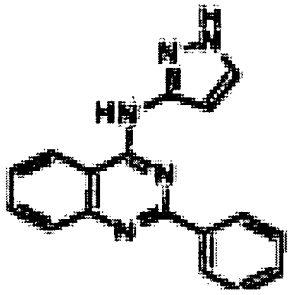

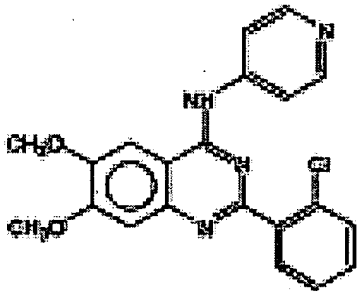

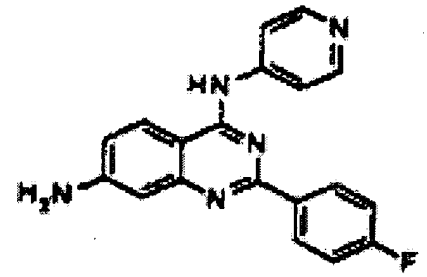

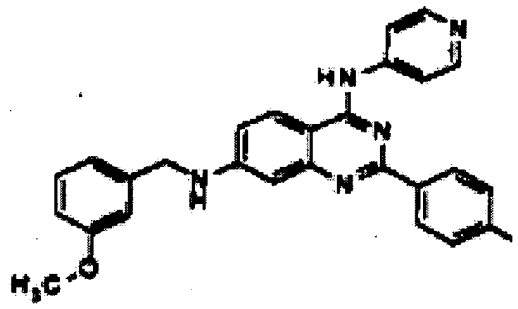

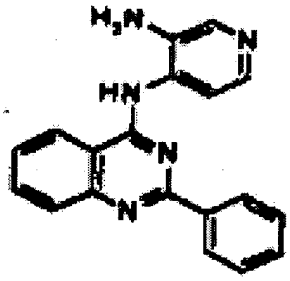

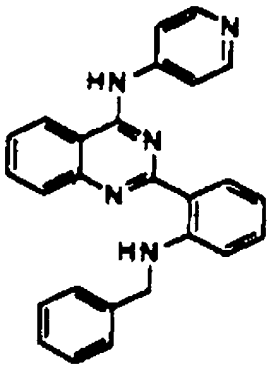

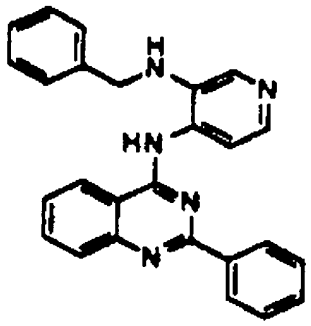

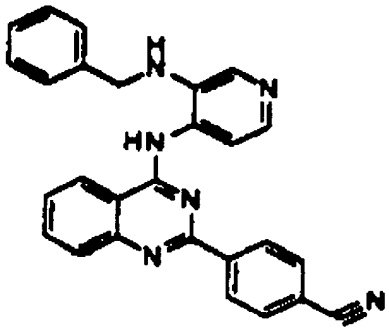

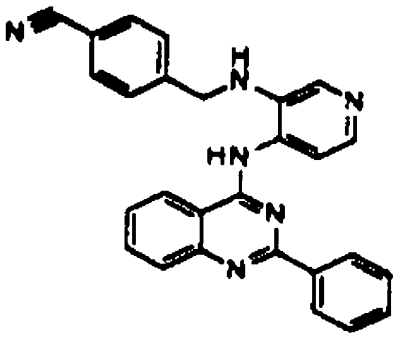

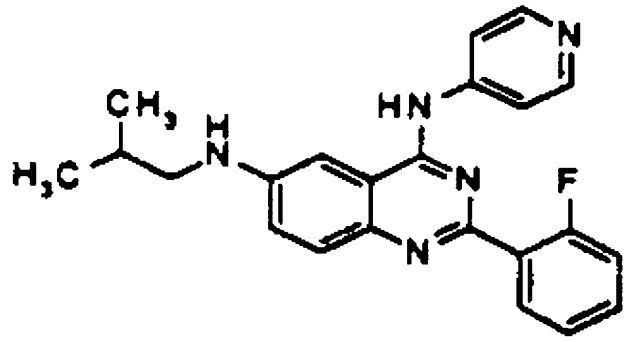

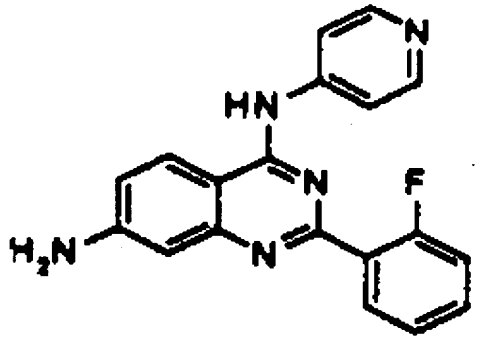

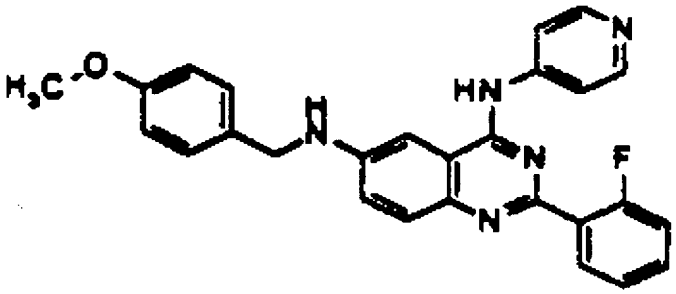

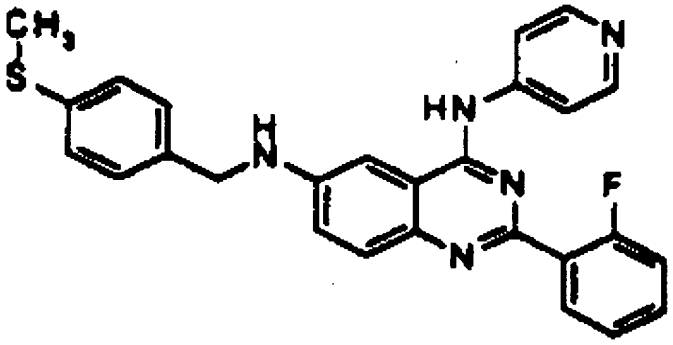

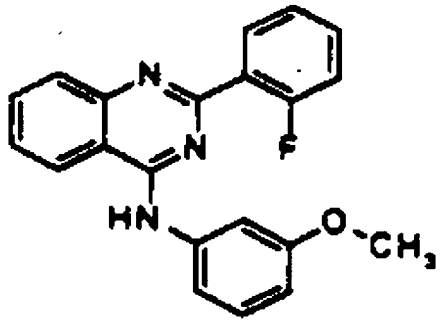

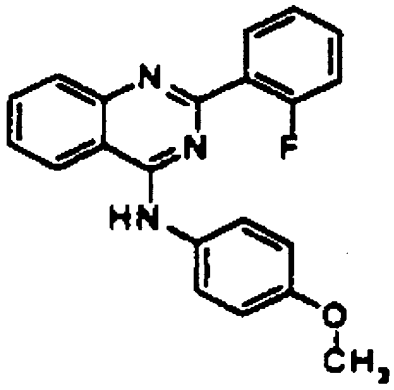

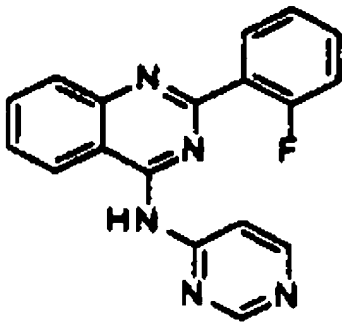

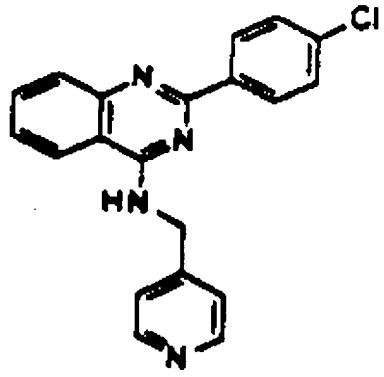
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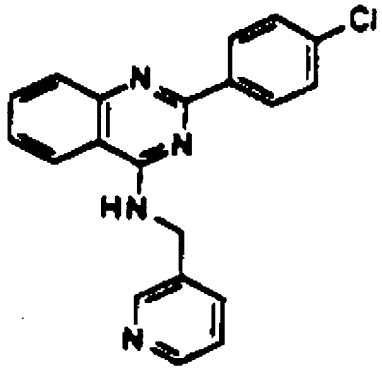
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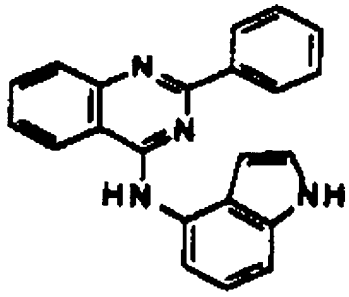
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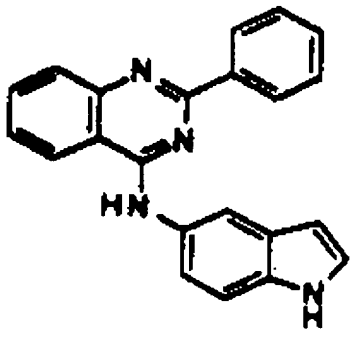
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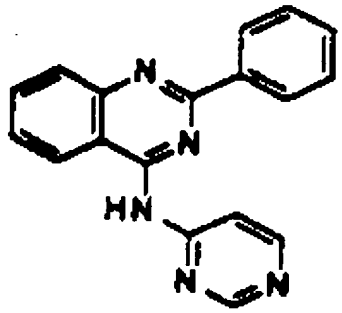
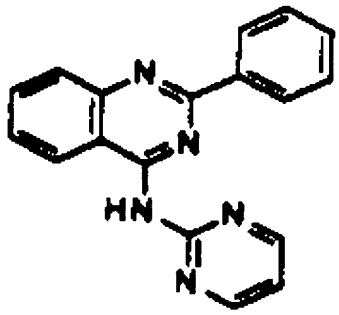
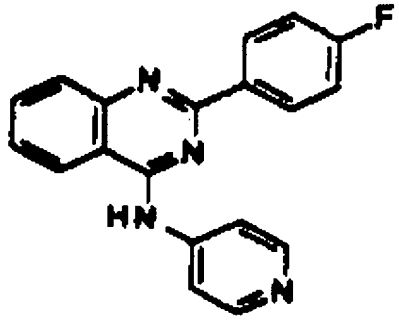
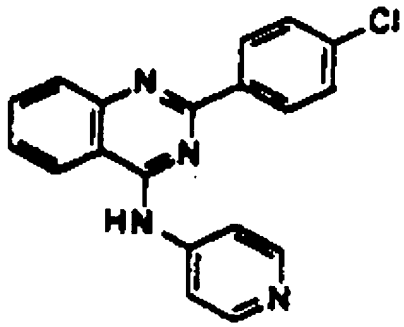








18-23. (canceled)

24. (previously presented): The method of claim 1 wherein the compound of formula 1 is selected from the group consisting of

2-phenyl-4-(4-pyridylamino)-quinazoline;

2-(2-bromophenyl)-4-(4-pyridylamino)-quinazoline;

2-(2-chlorophenyl)-4-(4-pyridylamino)-quinazoline;

2-(2-fluorophenyl)-4-(4-pyridylamino)-quinazoline;

2-(2-methylphenyl)-4-(4-pyridylamino)-quinazoline;

2-(4-fluorophenyl)-4-(4-pyridylamino)-quinazoline;

2-(3-methoxyanilyl)-4-(4-pyridylamino)-quinazoline;

2-(2,6-dichlorophenyl)-4-(4-pyridylamino)-quinazoline;

2-(2,6-dibromophenyl)-4-(4-pyridylamino)-quinazoline;

2-(2,6-difluorophenyl)-4-(4-pyridylamino)-quinazoline;

2-(2-fluorophenyl)-4-(4-pyridylamino)-6, 7-dimethoxyquinazoline;

2-(4-fluorophenyl)-4-(4-pyridylamino)-6, 7-dimethoxyquinazoline;

2-(2-fluorophenyl)-4-(4-pyridylamino)-6-nitroquinazoline;

2-(2-fluorophenyl)-4-(4-pyridylamino -6-aminoquinazoline;

2-(2-fluorophenyl)-4-(4-pyridylamino)-7-aminoquinazoline;

2-(2-fluorophenyl)-4-(4-pyridylamino)-6-(3-methoxybenzylamino)-quinazoline;

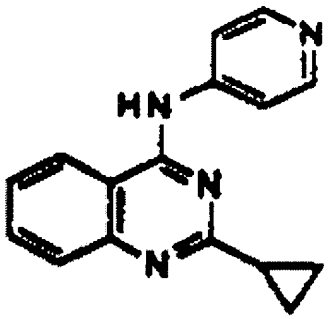
2-(2-fluorophenyl)-4-(4-pyridylamino)-6-(4-methoxybenzylamino)-quinazoline;

2-(2-fluorophenyl)-4-(4-pyridylamino)-6-(2-isobutylamino)-quinazoline; and

2-(2-fluorophenyl)-4-(4-pyridylamino)-6-(4-methylmercaptobenzylamino)-quinazoline.

25-33. (canceled)

34. (previously presented): A method to inhibit p38α activity, which method comprises contacting said p38α with a compound selected from the group consisting of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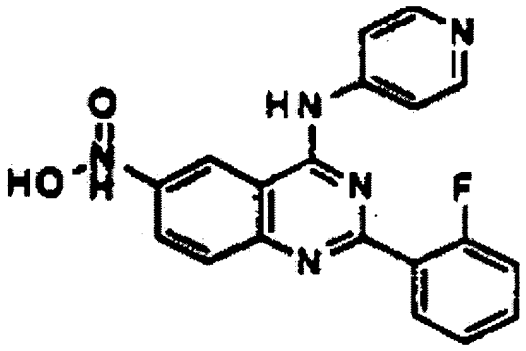
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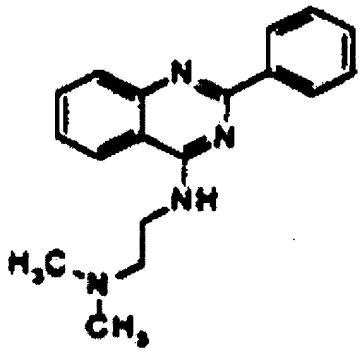

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